Allergy Abstracts

Editor
MURRAY M. ALBERT
Brooklyn, N. Y.

Editorial Board

KATHERINE BOWMAN
Brooklyn, N. Y.

HAROLD J. FRIEDMAN
Cleveland, Ohio

BERNARD B. SIEGEL
Far Rockaway, N. Y.

Associate Editors

ROBERT A. CHAIT
Rockville Centre, N. Y.

EUGENE H. WALZER
Bridgeport, Conn.

ELOISE KAILIN
Washington, D. C.

ISRAEL GLAZER
Tel-Aviv, Israel

RICHARD D. WISEMAN
Syracuse, N. Y.

MONROE COHEN
Brooklyn, N. Y.

JEROME SHERMAN
Baltimore, Md.

Advisory Editor
MATTHEW WALZER
Brooklyn, N. Y.

From the Allergy Division of
The Jewish Hospital of Brooklyn

Volume 19, Number 1 January, 1954

Announcement

Allergy Abstracts has been published since 1936 by members of the Allergy Division of The Jewish Hospital of Brooklyn. The Editorial Board is comprised of former residents of this department who contribute their services.

Allergy Abstracts selects and abstracts those articles in the literature which may be of clinical or theoretical interest to workers in the field of allergy. Each abstract represents a summary of the author's findings and views, and its inclusion in Allergy Abstracts does not imply approval of its contents by the editor.—*The Editors.*

Asthma and Hay Fever

Fatal Anaphylaxis in Bronchial Asthma Following Administration of Penicillin. Report of Two Cases With Autopsy Findings. Curphey, T. J.: New York State J. Med. **53**: 1107, 1953.

A 43-year-old woman was given 300,000 units of procaine aqueous penicillin intramuscularly for the treatment of a purulent postnasal drip and

pharyngeal infection. Two or three minutes later, she complained of tightness in her chest and dryness of the throat. She failed to respond to 0.3 c.c. of Adrenalin administered subcutaneously. Her breathing became stertorous, she developed marked cyanosis and lapsed into unconsciousness. One-half cubic centimeter of Adrenalin 1:1,000 was given intravenously with no effect. Within five minutes following the penicillin injection she expired. She was known to have had bronchial asthma for many years. "There was a history of allergy to penicillin in oil." During the past year, however, she had received procaine aqueous penicillin by injection on three or four occasions without untoward effects. Post-mortem examination revealed lungs which were hyperventilated and voluminous. The bronchi showed acutely congested mucosal surfaces and there was abundant tenacious mucoid exudate in the larger bronchi. The liver, kidney, spleen, pancreas, and brain were markedly congested. Microscopic examination revealed a bronchial submucosal infiltration of round cells and occasional eosinophiles and polynuclears. Sections taken from different lobes showed marked congestion of the capillary septa with patchy and irregular dilatation of the alveoli. The alveoli were free from edema or exudate. The smooth muscles of the walls of the bronchioles were not hypertrophied, nor was there any mucoid exudate in the lumina.

The second patient was a 63-year-old man with a long-standing history of bronchial asthma and bronchiectasis. He had received penicillin on several occasions, but none during the past four years. While in an asthmatic attack, he was given an intramuscular injection of 400,000 units of crystalline penicillin and 0.5 Gm. of streptomycin in distilled water. Shortly thereafter, the asthma became worse and was not relieved by 2 injections of Adrenalin. He then had a convulsion and expired within ten minutes after the penicillin injection. The lung on cut section showed firm granular raised areas of pinkish red tissue which sank in water. Other areas of the lung showed a mottled light and dark red surface. The bronchial mucosa was congested and the smaller bronchioles were distinctly dilated. Many plugs of tenacious inspissated mucus were noted in the small bronchi. There was no evidence of a coronary occlusion. Sections of the bronchi showed the lumina to be filled with mucus containing many eosinophiles and polynuclear cells. The bronchial walls and peribronchial tissue were densely infiltrated with round cells and eosinophiles. There was no significant hypertrophy of the smooth muscle coat. The peribronchial vessels and septal capillaries were dilated and congested. Many alveoli were filled with the same type of mucus noted in the bronchioles. The spleen, liver, and bone marrow showed marked eosinophilic infiltration. B. S.

Otorhinology and Ophthalmology

Further Observations on the Local Use of Cortisone in the Nose in Allergic Rhinitis. Dill, J. L., and Bolstad, D. S.: Tr. Am. Acad. Ophth. **56**: 214, 1952.

Cortisone in 1:4 dilution was applied as a spray four times daily to the nasal mucosa of 35 patients with allergic rhinitis for varying periods up to a year. Fourteen of these patients had nasal polyps. Fifty per cent of the patients showed marked improvement both subjectively and objectively, but symptoms reappeared within a short time after the spray was discontinued. In only one case did nasal polyps disappear. Nasal smears before and after treatment showed considerable variation in the number of eosinophiles found.

Biopsies of nasal tissue before and after local cortisone therapy showed no significant changes. It is concluded that, while cortisone nasal spray can produce relief of nasal symptoms in some cases, it should not replace specific allergic therapy. C.

Miscellaneous Allergies

Cerebral Complications of Serum Sickness. Park, A. M., and Richardson, J. C.: Neurology **3.** 277, 1953.

The neurological complications of serum sickness are reviewed. The most common type of involvement of the peripheral nervous system is serum neuritis. The brachial plexus is the site usually affected, although any peripheral nerve may be involved. Cranial nerve lesions due to serum sickness have also been described. A more generalized polyneuritis resembling the Guillain-Barré syndrome or acute ascending paralysis of the Landry type has also been seen with serum sickness. Pure spinal lesions with paraplegic signs have not been recorded. The most common type of cerebral involvement in serum sickness is the diffuse variety. The authors report the case of a 19-year-old man who developed typical signs of serum sickness five days after receiving antitetanus serum. He developed a severe headache and was apathetic. The cerebrospinal fluid was under slightly increased pressure and contained 14 lymphocytes per cubic millimeter, but the protein was normal. The electroencephalogram showed a widespread abnormality, particularly in the right central region. Signs and symptoms disappeared rapidly with cortisone therapy. However, shortly thereafter, he began having attacks of blurred vision; objects would dance and he would sway. After six weeks, these attacks became less frequent and finally ceased. Cases have also been reported in which cerebellar signs and even choreiform movements have developed with serum disease. Focal cerebral injury is one of the rarest manifestations of nervous system damage in serum sickness. Two such cases are reported. One patient, a 37-year-old man, became drowsy and then developed urticaria eight days after receiving antitetanus serum. Several hours later, he suddenly became unconscious and remained in a semicomatose state for the next forty-eight hours. When he regained consciousness, eleven days after the injection, he had a complete right hemiplegia, aphasia, hemianesthesia, and homonomous hemianopsia. Examination of the cerebrospinal fluid was normal. Arteriograms showed a normal vascular tree. Electroencephalogram demonstrated a gross dysfunction of the entire left hemisphere. On one occasion, he developed a grand mal seizure, beginning focally in the right arm and then becoming generalized. Although slight improvement was noted in the power of his leg and in his speech, the remaining neurological findings persisted even after months of observation. It would appear, in this case, that a transient vascular occlusion occurred, but the secondary cerebral damage was irreversible.

The authors report a second case with similar focal cerebral injury with serum sickness. In this case, the damage was less severe and good functional recovery occurred. It is postulated that the blood vessels in the wall of the major cerebral arteries are the seat (i.e., shock-organ) of the allergic reaction, in the focal type of cerebral lesions. B. S.

Allergic Reactions to Therapeutic Agents: Treatment With Adrenocorticotropic Hormone (ACTH) or Cortisone. Shulman, L. E., Schoenrich, E. H., and Harvey, A. Mc.: Bull. Johns Hopkins Hosp. **92**: 196, 1953.

Twenty-four patients with allergic reactions to various therapeutic agents were treated with ACTH, intravenously or intramuscularly, or with oral

cortisone. Only 7 of the patients had arthritic symptoms. Thirteen of the reactions were caused by penicillin, 8 by horse serum, and 1 each by sulfonamides, parasalicylic acid, and gold salts. Most of the reactions were mild and of an urticarial nature. Previous medications, such as Adrenalin, antihistamines, and intravenous procaine (in one patient), failed to produce improvement. The average total dose of cortisone administered was 760 mg. The individual amounts ranged from 350 to 1,050 mg. The length of treatment varied from two to seven days. Within forty-eight hours following the administration of either cortisone or ACTH, the patients were usually much improved and many obtained relief from itching within a few hours after treatment was initiated. In those patients treated with ACTH, intravenous administration of the hormone provided the most rapid relief. Two patients with reactions from horse serum showed symptoms and laboratory findings indicating central nervous system involvement. Both of these patients responded to therapy. Of 600 individuals who have been given ACTH in Johns Hopkins Hospital during the past three years only 5 patients had a reaction to it. Hormone derived from beef and from pork was used in these patients; the more severe reactions seemed to occur from the beef variety. The authors conclude that large intensive doses of oral cortisone are the simplest, most effective, and least expensive method of treatment for severe drug reactions.

R. W.

Dextran—an Antigen in Man. Kabat, E. A., and Berg, D.: J. Immunol. **70**: 514, 1953.

Dextrans, the polysaccharides synthesized from sucrose by *Leuconostoc mesenteroides* which cross react specifically with Types II, XII, and XX horse and rabbit antipneumococcal sera, have caused allergic reactions in man when given intravenously as a plasma expander. Quantitative immunochemical studies were carried out with dextran to determine its antigenicity in man. Among normal human beings who had received 1 mg. of dextran subcutaneously, many had developed precipitins within three weeks. Cutaneous sensitivity of the immediate wheal and erythema type also developed in some, but this sensitivity could not be passively transferred. In rabbits and guinea pigs, neither precipitins nor active anaphylactic sensitization could be produced. Differences in immunologic behavior of various antisera with native and partially hydrolyzed dextrans were shown to depend on structural differences among the preparations.

Dextran is present as a contaminant of all commercial sugar and also can be elaborated by microorganisms in the gastrointestinal tract. It was suggested that such prior contact with dextran might account for the immunologic and systemic allergic responses in individuals not previously injected with dextran.

M. Cohen.

Cortisone Therapy of Penicillin Reactions. Davis, J.: New York State J. Med. **53**: 69, 1953.

Five cases of penicillin hypersensitivity are reported. Two patients developed urticaria, two developed erythema, and one patient had an erythema multiforme-like eruption. These patients did not respond to treatment with antihistamines, ephedrine, adrenaline, calcium gluconate, and ACTH (1 case). An intramuscular injection of 50 mg. of cortisone was given to each patient after symptoms had been present for from four to ten days. In each case, there was a symptomatic response in from five to eight hours. In several cases, a second injection of cortisone was given within twenty-four hours.

Relief of symptoms was complete in each case within twenty-four to forty-eight hours. Remissions were not noted in this series. B. S.

Prevention of Allergic Transfusion Reactions. Ferris, H. E., Alpert, S., and Coakley, C. S.: New York State J. Med. **53**: 539, 1953.

One cubic centimeter of Pyribenzamine, containing 25 mg., was added to the blood to be transfused in a series of 607 blood transfusions. In this group, there was one allergic reaction, no pyrogenic reactions, and one hemolytic reaction. In a control series of 742 transfusions in which no antihistamines were used, 21 allergic reactions and 32 pyrogenic reactions were noted. The absence of pyrogenic reactions in the experimental series suggests that these reactions are probably allergic in nature and are the result of a response to histamine liberation. The hemolytic reaction, which is not a histamine reaction, was not masked by the use of antihistamine. B. S.

Loeffler's Syndrome Following Penicillin Therapy. Reichlin, S., Loveless, M. H., and Kane, E. G.: Ann. Int. Med. **38**: 113, 1953.

A 26-year-old man was treated for syphilis twice weekly with injections of procaine penicillin in sesame oil with aluminum monostearate. After the fourth injection, he developed a local reaction which lasted two days. Following the next injection, he developed a local reaction and generalized urticaria, which responded to tripelennamine hydrochloride. He was given the same antihistamine prior to the next two injections of penicillin and did not develop urticaria. However, after the last injection, he did have a dry sore throat and a painful burning paroxysmal cough which lasted for about two days. These symptoms plus chills and fever recurred after the next penicillin injection and he was admitted to the hospital. He had taken penicillin lozenges two years before with no untoward effects. He gave a history of having had hay fever in childhood. On admission, his temperature was 39.6° C. and he was flushed. He had dermographia and a dry, nonproductive cough. Scattered crepitant râles were heard in his chest. The white count was 23,150 per cubic millimeter with 4 per cent eosinophiles. The Kolmer Wassermann test was 4 plus. The chest x-ray showed a diffuse, mottled infiltration throughout both lungs. The only therapy given was an antihistamine for urticaria. His temperature dropped to normal in five days. On the third day, he developed giant urticaria at the sites of previous penicillin reactions. The following day, he had a diffuse erythematous maculopapular eruption. The infiltrations in the lung disappeared by the end of the second week. The percentage of eosinophiles in the peripheral blood increased rapidly. The highest degree of eosinophilia occurred on the sixth hospital day with 80 per cent eosinophiles and a total white count of 42,900 per cubic millimeter. A study of the sternal marrow on the third day revealed a total count of 138,000 per cubic millimeter and 52 per cent eosinophiles. Intracutaneous tests with 20,000 units of crystalline penicillin, type G, evoked a moderate or two-plus reaction. The positive skin reaction could not be repeated when attempted about two weeks later. Control tests with saline were negative on both occasions. Intracutaneous tests with procaine penicillin and scratch tests with the vehicle, sesame oil with aluminum monostearate, gave negative reactions. B. S.

Urticaria Due to Drugs of the Digitalis Series. Wolfe, L. S., and Geiger, A. J.: New England J. Med. **248**: 148, 1953.

An 82-year-old woman with congestive heart failure developed urticaria following the administration of each of the following digitalis preparations:

whole leaf digitalis, digitoxin, digoxin, Digilanid, lanatoside C, and squill glycoside. When digitalization was induced within 48 hours or less, symptomatic improvement resulted without the immediate development of urticaria. However, when the digitalis was continued, generalized urticaria appeared and the lesions became worse with the continuation of therapy. Antihistamines relieved the itching but did not abolish the reaction. The rapidity of the disappearance of the urticaria after the drugs were discontinued was roughly proportional to the average duration of action of each of the preparations: two weeks after digitalis, one week after digitoxin, and a few days after digoxin and lanatoside C. On two occasions, the patient also developed urinary frequency and urgency, with prolapse of the urethral meatus. Cystoscopic examination showed a dusky edema of the bladder which was interpreted as an allergic cystitis. This disappeared when the digitalis was stopped. There was no associated eosinophilia with these reactions. Scratch and patch tests with the digitalis products gave negative reactions. Since urticaria occurred following the administration of highly purified as well as crude preparations from three different plant sources (*Digitalis purpurea, Digitalis lanata,* and squill), it is suggested that the allergic response in this case was probably due to the cyclopentenophenanthrene nucleus, which is common to all these cardiotonic glycosides. B. S.

Anaphylaxis

Anaphylactic Reactions and Concentrations of Antibody in Rats and Rabbits: Effect of Adrenalectomy and Administration of Cortisone. Dews, P. B., and Code, C. F.: J. Immunol. **70**: 199, 1953.

Adrenalectomized rats sensitized to horse serum were found to be more susceptible to anaphylaxis than similarly sensitized intact animals. Adrenalectomy, performed prior to sensitization, resulted in greater anaphylactic sensitivity than that resulting when the operation followed sensitization. Adrenalectomy, however, did not lead to higher concentrations of hemolysins after immunization. It is suggested, therefore, that the development of anaphylactic sensitivity in rats is affected by the presence of the adrenal glands and is not related to their effect on antibody concentration. Cortisone, administered immediately before the challenging dose, increased the resistance of adrenalectomized rats to anaphylactic shock although severe reactions occurred. When cortisone was given during sensitization, the degree of sensitivity was reduced so that much milder anaphylactic reactions resulted. This occurred even when cortisone was discontinued eighteen days prior to challenge and was no longer present in the tissues when the animals were tested.

In rabbits, local anaphylaxis was induced in normal and adrenalectomized animals by daily injections of egg albumin or bovine gamma globulin. Adrenalectomy had some enhancing effect on cutaneous sensitivity. Administration of cortisone to both groups of animals produced a pronounced diminution in the concentrations of circulating antibodies and reduced the severity of the cutaneous lesions. The inhibiting effect of cortisone on cutaneous sensitivity in rabbits may well be accounted for by this reduction in circulating antibodies. M. Cohen.

Study With Fluorescent Antibody of Fate of Intradermally Injected Proteins in Rabbits. Waksman, B. H., and Bocking, D.: Proc. Soc. Exper. Biol. & Med. **82**: 738, 1953.

Normal and sensitized rabbits received intracutaneous injections of crystalline egg albumin and bovine gamma globulin. The injected areas of

the skin and the homolateral popliteal lymph nodes of each rabbit were removed at various intervals and quick frozen. These tissues were stained with fluorescein-labeled homologous antibody and studied under the fluorescence microscope. The amount of antigen present in the tissues was evaluated by the intensity of staining with fluorescent antibody and the extent of antigen distribution.

In normal rabbits, antigen was taken up by histiocytic cells both locally and in the sinuses of the draining lymph node. Considerable quantities remained extracellular and were presumed to diffuse away to be dealt with elsewhere in the body. Polymorphonuclear cells participated actively in the skin responses but did not contain intact antigen. However, many lymphoid cells in the draining node were seen to contain antigen.

In the passively sensitized animals and, to a greater extent, in those sensitized with Freund's adjuvants, antigen disappeared more slowly from the skin sites and draining nodes than in the normal rabbits. Adjuvant sensitized animals showed increased phagocytosis of antigen. It was suggested that the diffusion of antigen into the general circulation was retarded in sensitized animals, either by local edema or by combination with antibody.

M. Cohen.

Pharmacology, Physiology, and Pathology

A Study of the Effects of Sodium Salicylate and Some Structurally Related Compounds on Antigen-Antibody Reactions in Vitro. Friend, C.: J.: Immunol. **70**: 141, 1953.

The effect of sodium salicylate and various related chemicals upon in vitro antigen-antibody reactions was investigated. Egg albumin and anti-egg albumin rabbit serum and pneumococcal polysaccharide type III and antipneumococcus type III rabbit serum were the antiprotein and anti-polysaccharide systems studied. The compounds to be studied were added to predetermined amounts of antigen and antiserum. After a period of incubation, the precipitates were analyzed for antibody nitrogen. It was found that the addition of increasing amounts of salicylates to constant amounts of antigen and antiserum produced a corresponding decrease in the amount of precipitable antibody nitrogen. Increasing the amount of salicylate resulted in an increased dissolution of precipitate even after the combination of antigen and antibody had taken place. After thoroughly washing the precipitate, salicylate could not be detected. This suggested that the compound was not incorporated in the precipitate. After removal of the salicylates by dialysis, it was possible to recover an appreciable amount of antibody, indicating that the inhibition of precipitation by salicylates was partially reversible. The length of time or the temperature at which salicylates were exposed to the antigen-antibody system had no noticeable effect on the amount of precipitate formed. The rate of flocculation was not affected by simply increasing the volume or changing the salt concentration unless salicylate was added simultaneously, and then it materially decreased. All 3 of the hydroxybenzoic acids (ortho, meta, and para) as well as o-methoxybenzoic acid significantly retarded the precipitation of antigen and antibody in the two systems under investigation. Since inhibition also occurred with o-chloro and m-chlorobenzoic acids, it is suggested that specificity due to chemical structure is not responsible for the inhibition of the precipitation of antigen and antibody. Although the concentrations used in the above experiments far exceeded levels usually attained in human beings, it is implied that similar mechanisms may be responsible for the effect obtained when patients are given salicylate therapy. The author con-

cludes that inhibition of in vitro antigen-antibody precipitation by salicylates probably is due to an increase in the solubility of the antigen-antibody complex. R. W.

A Comparative Histologic and Immunologic Study in Rabbits of Induced Hypersensitivity of the Serum Sickness Type. Germuth, F. G.: J. Exper. Med. **97**: 257, 1953.

A single intravenous dose of crystallized bovine serum albumin was injected into 76 rabbits. A skin test with 1 mg. of antigen was also made the day before the animal was sacrificed. Blood was drawn at various intervals after the injection and the antigen content of the serum was determined. Quantitative tests for antibody were also carried out. Animals were sacrificed from six to twenty-eight days after injection.

Antigen was removed from the blood in 3 phases. Circulating antigen was present in all animals for ten days. "By the 12th day, approximately 30 per cent ($^{12}/_{37}$) of the rabbits had eliminated the antigen and produced measurable quantities of circulating antibody. By the 18th day, 7 per cent ($^{1}/_{14}$) of the animals continued to show traces of antigen while 93 per cent ($^{13}/_{14}$) had developed considerable levels of antibody . . ." The first phase of antigen disappearance is interpreted as equilibration of antigen with vascular and extravascular body fluids. The second phase, a slower rate of disappearance, is interpreted as that of normal catabolism. The third very rapid phase of loss of antigen correlates with the appearance of antibody at the tenth to twelfth day. Tissue lesions in the spleen appeared on the sixth day and reached a maximum on the eleventh day. Since it is presumed that the immune phase antedates the actual finding of free antibody in the serum, and since "the extent of the splenic lesions in rabbits killed on the 12th day was inversely proportional to the magnitude of the serum antigen or antibody concentrations . . . this correlation supports the interpretation that the splenic lesions result from the immune phase of antigen elimination." Glomerular lesions showed similar time correlations. These tissue lesions regressed after the elimination of antigen. Arthus reactions appeared slightly later than the other lesions and this is explained as being due to the reaction of circulating antibody with antigen introduced in the skin. The other tissue lesions occurred at a time when antigen was still circulating and antibody was just being formed but was not yet in sufficient excess to allow detectable blood levels.

Tissue lesions observed included focal inflammatory intimal reactions in pulmonary arteries and aorta in 72 per cent of the animals, arteritis similar to periarteritis nodosa in 51 per cent, endocarditis in 54 per cent, and glomerular changes in over 80 per cent of the animals. The latter finding was surprising inasmuch as previous workers using a dose of albumin 4 times greater found little nephritis. The dose of antigen thus may prove important to the incidence and type of lesions. In addition to the lesions commonly associated with hypersensitivity reactions, granulomatous lesions were observed in spleens and lymph nodes on or about the twelfth day. These lesions were noted shortly before the appearance of cardiovascular and renal lesions, possibly because of antibody formation at these sites. The splenic lesions regressed very rapidly, becoming infrequent and slight by the fifteenth day, while glomerular and arterial changes were prominent. It is suggested that "the widespread granulomatous foci encountered in some cases of polyarteritis nodosa might represent a response of the focal lymphocytic infiltration to repeated or prolonged exposure to antigen." K.

Respiratory Acidosis—Pathogenesis and Treatment. Segal, M. S., Dulfano, M. J., Herschfus, J. A., and Shanks, J. A.: Ann. Allergy **11**: 206, 1953.

Uncompensated respiratory acidosis, rather than the accumulation of carbon dioxide (hypercapnia), is the cause of the so-called carbon dioxide intoxication syndrome. This conclusion is based on the fact that, until breakdown of the acid base, homeostasis occurs with resulting decrease in pH and symptoms do not appear even in the face of prolonged hypercapnia. Many patients with chronic pulmonary emphysema have chronically elevated blood CO_2 levels but do not manifest the syndrome until, through some superimposed respiratory difficulty, there is a decrease in the blood pH.

Respiratory acidosis frequently develops in chronic pulmonary emphysema. Respiration in such patients is maintained chiefly through hypoxic stimulation of the respiratory center. When high concentrations of oxygen are administered to such patients, the main stimulus to respiration is removed. Respiration and ventilation then decrease markedly and the CO_2 level rises, but the compensatory mechanisms maintain the pH within normal range. However, if ventilation and effective gas exchange remain impaired, adequate compensation cannot be maintained and the pH falls below normal levels with resulting respiratory acidosis. Respiratory acidosis may occur as a result of chronic organic or functional lung diseases or as a result of acute respiratory insufficiency from various causes. Most commonly, however, it develops in chronic organic lung disease, particularly when associated with chronic hypoxia, but poor alveolar ventilation and ineffective gas exchange are the basic causes of the condition. Diagnosis, although suggested by the symptomatology, can be definitely made only by laboratory determinations of the arterial partial pressure of CO_2. Patients who may possibly develop this condition should not be given high concentrations of oxygen or drugs which might depress the respiratory center. Symptomatic treatment, once the syndrome has developed, consists of the use of such measures as mechanical respirators, electrophrenic stimulation, artificial pneumoperitoneum, a graded program of oxygen therapy, and such etiologic measures as indicated, i.e., the use of Nalline or picrotoxin to combat drug intoxication. Since respiratory acidosis is basically due to ineffective alveolar ventilation, treatment must be aimed mainly at maintaining and promoting adequate alveolar ventilation. F.

The Release of Histamine by Egg White in Non-Sensitized Animals. Schachter, M., and Talesnik, J.: J. Physiol. **118**: 258, 1952.

Both fresh and boiled egg white solutions were injected intravenously into rats, cats, and dogs. Histamine plasma levels were measured by assays done on isolated atropinized guinea pig ileum. Egg white solutions were also injected into the artery of isolated perfused flaps of skin and the blood leaving these tissues was measured for its histamine content. Following a single intravenous injection of crude but not boiled egg white, cats showed an immediate rise in histamine blood levels. A similar response was also obtained from the skin flaps in the cat. In rats, a single intravenous injection of either crude or boiled egg white raised the histamine blood level. In unsensitized dogs, neither local nor systemic intravascular injections produced a rise in histamine blood levels. It is suggested that egg white contains 2 antigens and that the heat stable component is the ovomucoid fraction. The authors concluded that egg white, like horse serum, is a foreign protein capable of releasing histamine without previous sensitization. R. W.

A Comparison of the Effects of L-Nor-Epinephrine, Synthetic L-Epinephrine, and U.S.P. Epinephrine Upon Cerebral Blood Flow and Metabolism in Man. Sensenbach, W., Madison, L., and Ochs, L.: J. Clin. Invest. **32**: 226, 1953.

Adult men were studied by the nitrous oxide method to determine the effect on cerebral blood flow of l-nor-epinephrine, synthetic l-epinephrine, and U.S.P. epinephrine in oil (contains some nor-epinephrine in addition to l-epinephrine). The doses used varied from 600 to 1,400 μg and were administered intramuscularly. Cerebral blood flow was measured before and twenty minutes after drug administration; 3 additional measurements were also taken in the next ten to twenty minutes. Blood pressure was not affected by more than a few millimeters, in any case. The cerebral vasoconstriction produced by l-nor-epinephrine exceeded the increase in perfusion pressure, thus decreasing blood flow to the brain. However, cerebral oxygen consumption was not decreased because the brain extracted oxygen from arterial blood more efficiently. There was "a significant increase in arterial O_2 content . . . and a decrease in cerebral venous oxygen content. . . . Mean arterial CO_2 content decreased significantly . . . apparently as a result of mild hyperventilation." Synthetic l-epinephrine and U.S.P. epinephrine did not change cerebral hemodynamics. K.

Persistence of Histaminic Responses in the Human During Cholinesterase Administration. Barnard, R. D., Stanton, H. T., Jr., and Goldman, B.: Ann. Allergy **11**: 170, 1953.

Large intravenous doses of a purified human cholinesterase failed to alter both the skin and gastric secretion reactions to histamine in guinea pigs and human beings. They also did not affect the vasodepressor reaction of histamine in the cat. These observations suggest that investigations should be made to determine the role played by the acetylcholine-cholinesterase system as opposed to the histamine-antihistamine system in the various hypersensitivity states. F.

Cross-Sensitivity to Diphenylhydantoin Sodium and to Phenobarbital. Report of Two Cases. Morris, G. E., and Cohen, J. D.: New England J. Med. **248**: 27, 1953.

One patient developed a dermatitis medicamentosa due to phenobarbital after taking the drug for two years. After the eruption had cleared, diphenylhydantoin sodium was given and within forty-eight hours the rash reappeared. The second patient developed a dermatitis medicamentosa after taking diphenylhydantoin sodium for one month. After the eruption cleared, phenobarbital was given and within twenty-four hours she had a recurrence of the rash. The authors state that these cases represent cross-sensitization to the two drugs and demonstrate the similarity in their chemical structures. B. S.

The Comparative Retention of Antigen in the Skin of Immune and Normal Rabbits as Determined With Egg Albumin Labeled With Radioactive Iodine. Korngold, L., Stahly, G. L., Dodd, M. C., and Myers, W. G.: J. Immunol. **70**: 345, 1953.

Radioactive iodine, I^{131}, was chemically attached to crystallized hen ovalbumin to form a radioactive antigen. By means of a Geiger-Mueller counter, the rate of disappearance of radioactivity from cutaneous sites of injection in

rabbits was measured. The specificity of the ovalbumin was not altered by this chemical treatment since the iodinated and untreated ovalbumins were precipitated by antiserum to the same degree.

Rabbits were immunized by a series of cutaneous injections of iodinated ovalbumin and the sites of injection were tested after twenty-four hours. A retention of antigen was found at sites where an inflammatory reaction developed and this increased progressively with the amount of inflammation. Immunized animals showed an increased dermal retention of radioactive antigen during the anamnestic response evoked by injection of the antigen. In these animals, the local inflammatory (Arthus) response was greater and antigenic retention by the skin developed more rapidly than during the original course of immunization. Thus, there appeared to be a correlation between the ability to produce an Arthus reaction and the capacity of the skin to retain the antigen. M. Cohen.

A Quantitative Comparison of Antibody Produced by X-Radiated and Normal Rabbits. Maurer, P. H., Dixon, F. J., and Talmage, D. W.: Proc. Soc. Exper. Biol. & Med. **83**: 163, 1953.

Rabbits were exposed to 400 r whole body irradiation prior to, or simultaneously with, immunization, in order to interfere with the early radiosensitive phase of antibody production. No immunochemical alteration in the character of the serum antibody occurred in the x-irradiated animals, although the concentration of the antibody was greatly reduced.

Another group of rabbits was irradiated with 800 r after immunization, producing maximal radiation injury so that a large part of the lymphoid and hematopoietic tissue of these animals was destroyed. Nevertheless, they were able to synthesize normal amounts of antibody which did not differ immunochemically from antibody produced by nonradiated animals. These findings are consistent with the concept that the synthesis of antibody may occur in radioresistant cells or tissues. M. Cohen.

Effect of Stress on Diurnal Fluctuations in Eosinophils of the Laboratory Mouse. Louch, C., Meyer, R. K., and Emlen, J. T.: Proc. Soc. Exper. Biol. & Med. **82**: 668, 1953.

Mice kept in a continuous environment of 3° C. showed a significantly smaller number of circulating eosinophils than did those kept at room temperature. However, the normal diurnal fluctuation in the number of circulating eosinophils was maintained in the animals exposed to cold. It is suggested that the nocturnal eosinopenia occurring in mice is caused by their nocturnal activity which stimulates the adrenal glands. Exposure to cold apparently did not suppress adrenal function and therefore the diurnal eosinophil fluctuation was unaffected. M. Cohen.

The Stimulation of the Eosinophil Leucocyte. Vaughn, J.: J. Path. & Bact. **64**: 91, 1952.

Ascaris extract, when administered parenterally, stimulated the production of an eosinophilia in normal guinea pigs. This phenomenon is not mediated through the parasympathetic nervous system, since it was unaffected by the inhibition of the parasympathetic nervous system with atropine. The extract was shown to be a mixture of polypeptides and other protein breakdown products. The eosinophilogenic effect of the extract was completely inhibited by administration of an antihistaminic drug. Histamine was shown to have an eosinophilogenic effect similar to that of the extract. J. S.

Half-Lives of Homologous Serum Albumins in Several Species. Dixon, F. J., Maurer, P. H., and Deichmiller, M. P.: Proc. Soc. Exper. Biol. & Med. **83**: 287, 1953.

I^{131}-labeled homologous albumin was injected intravenously in human beings, cows, dogs, rabbits, and subcutaneously in mice. Bleedings were made at intervals and the concentrations of protein bound I^{131} in the plasmas were determined. The half-lives of I^{131}-labeled homologous albumins were: cows, 20.7 days; human beings, 15 days; dogs, 8.2 days; rabbits, 5.7 days; and mice, 1.2 days. When the metabolic rates of rabbits were elevated by giving them thyroxin, the albumin half-lives fell to 4.4 days. These results corresponded very closely to those obtained for gamma globulin half-lives in the same species. It was suggested that the catabolism of albumin and gamma globulin is dependent upon the metabolic characteristics of the host and not upon the characteristics of the protein molecules themselves. M. Cohen.

Miscellaneous

Studies on the Generalized Shwartzman Reaction. III. Lesions of the Myocardium and Coronary Arteries Accompanying the Reaction in Rabbits Prepared by Infection With Group A Streptococci. Thomas, L., Denny, F. W., Jr., and Floyd, J.: J. Exper. Med. **97**: 751, 1953.

The abdominal skin of rabbits was infected intracutaneously with group A streptococci. After varying time intervals, meningococcal or *S. marcescens* toxin was injected in the ear vein in doses sufficient to elicit a Shwartzman reaction in cutaneously prepared rabbits. Marked local Shwartzman reactions occurred in animals which had been infected with undiluted or 10^{-1} dilutions of streptococcus broth culture. With 10^{-2} dilutions milder reactions were noted. The optimal interval between infection and toxin administration was twenty-four hours. No reaction occurred when streptococci were injected twenty-four hours after the toxin injection. No reaction resulted when filtrates of streptococci or killed suspensions of streptococci were substituted for living organisms. Penicillin administered twelve hours prior to toxin administration prevented the appearance of the reaction. Concomitantly with the appearance of a severe skin lesion some animals died and were found to have the typical lesions of generalized Shwartzman reaction, namely, bilateral cortical necrosis of the kidneys. Administration of streptococci intravenously twenty-four hours prior to the injection of toxin greatly enhanced the incidence of generalized Shwartzman reactions. Animals given undiluted cultures reacted in this manner to toxin administration as long as five or six days thereafter. Smaller doses of bacteria left the animals in a prepared state for shorter periods of time. It was essential that bacteria be administered before the toxin and that the organisms be living. The renal lesions are described in detail as they developed over a period of hours. Varying degrees of necrosis and hemorrhage were found in lungs, liver, spleen, gastrointestinal tract, thymus, and lymph nodes as in the classic generalized Shwartzman reaction. When a program was carried out consisting of the administration of large doses of streptococci followed forty-eight hours later by 0.2 mg. *S. marcescens* toxin intravenously, half of the animals showed acute myofibril necrosis in the heart. In animals which survived a week, multinucleated giant cells and calcium were found about these necrotic areas as well as large basophilic mononuclear "inflammatory cells." Similar lesions were observed in animals subjected to two intravenous injections of meningococcal toxin. When the priming streptococcal dose was decreased, a different lesion was found within two days of the eliciting toxin injection. This "consisted of the

accumulation of masses of homogeneous, eosinophilic material with the staining properties of fibrinoid, within the substance of the arterial wall. When present in the media or adventitia, it was usually associated with varying degrees of necrosis of the wall; when confined to the intima, necrosis was less evident." This lesion could not be demonstrated in toxin-prepared, toxin-challenged animals, or in rabbits injected with either streptococci or toxin alone. The optimal bacterial dose necessary to produce cardiac fibrinoid necrosis lay within a narrow range. No correlation was observed between arterial fibrinoid necrosis and cortical necrosis of the kidneys. There was also an optimal dose and time for administration of meningococcal toxin. The incidence of fibrinoid necrosis was highest in animals dying between twenty-four and forty-eight hours after toxin administration. Fibrinoid necrosis was found in the absence of streptococcal bacteremia. The vascular fibrinoid material closely resembled the eosinophilic hyaline material found in the early stages of bilateral cortical necrosis and seemed to be derived from the blood rather than from capillary wall. It was observed that the fibrinoid degeneration lesion bore many points of resemblance to human lesions of rheumatic fever, disseminated lupus erythematosus, thrombotic thrombocytopenia, and periarteritis nodosa. K.

Poisoning by Methyl-Parafynol (Dormison) Fatal Suicidal Overdose of 3-Methyl-Pentyne-OL-3, A New Hypnotic. Cares, R. M., Newman, B., Mauceri, J. C.: Am. J. Clin. Path. **23**: 129, 1953.

A 45-year-old woman expired within one to three hours after ingesting from 18 to 24 capsules of Dormison. Autopsy disclosed a relatively good state of oxygenation of the tissues and moderate vascular and lung congestion. Death was attributed to cardiac arrest following coma resulting from acute Dormison poisoning. Toxicologic analysis disclosed the presence of Dormison in a concentration of 49 mg. per 100 Gm. of liver tissue (10 to 14 per cent of the ingested dose). The total fatal dose was from 90 to 120 mg. per kilogram of body weight. The acute oral LD_{50} for rats, mice, and guinea pigs is from 600 to 900 mg. per kilogram. It was concluded that Dormison is probably more toxic for human beings than for lower animals, that from 9 to 12 times the recommended dose of 2 capsules may prove fatal, and that the rapidity and mechanism of death is such that rescue measures are unlikely to save the patient who attempts suicide with this drug. K.

Allergic Factors in the Production of Leukemids. Goldblum, R. W., Bocobo, F. C., Curtis, A. C.: J. Invest. Dermat. **20**: 1, 1953.

The dermatitis which was present in 5 patients with either lymphatic leukemia or lymphosarcoma was studied to ascertain what factors might have produced the rash. Skin biopsies in all patients were essentially negative, only nonspecific inflammatory reactions having been observed microscopically. Intracutaneous tests with the various blood fractions of their own blood (albumin, globulin, red cells, and white cells) were made on three of the patients. Similar studies were made on 5 patients with Hodgkin's disease who did not have complicating skin manifestations and on 10 control patients without lymphogenous disease. Case 1, a patient with lymphatic leukemia, reacted quite strongly when tested intracutaneously with his own serum and globulin or with serum from Case 2, a patient with lymphosarcoma. Case 2 reacted with the serum from Case 1. All other direct tests yielded essentially negative reactions. All attempts to demonstrate passive transfer of the reactions were completely unsuccessful. In no instance could it be demonstrated

that the skin lesions present were due to sensitization to red or white blood cells. The authors conclude that leukemid reactions, if due to an allergic process, must be caused by fixed antibodies rather than by reagins. R. W.

The Treatment of Behavior Disorders in Children With Benadryl. A Preliminary Report. Effron, A. S., and Freedman, A. M.: J. Pediat. **42**: 261, 1953.

Elixir Benadryl was administered to 44 hospitalized children between the ages of 6 and 12 years with psychiatric disturbances. Sixty-one per cent of the patients showed improvement. Those with primary behavior disorders were most benefited. The most useful effect of the drug was its ability to reduce anxiety. The beneficial results observed could not be ascribed to the general trend of improvement occurring with hospital confinement, since the improvement surpassed that attained in untreated patients or in those treated with phenobarbital. No toxic symptoms were observed. J. S.

The Function of the Eosinophile Leukocyte. Vaughn, J.: Blood **8**: 1, 1953.

Groups of young guinea pigs were given intraperitoneal injections of either histamine acid phosphate or ascaris extract and then sacrificed one, three, six, twelve, or twenty-four hours later for histologic examinations. Adult guinea pigs with an eosinophilia, presumably from an infestation with intestinal parasites, as well as young healthy guinea pigs, were also examined at post mortem for comparative purposes. Eosinophile counts were done at six, twelve, and twenty-four hours and immediately before death. Only an occasional eosinophile was found in the tissues of normal young guinea pigs. Almost identical reactions were observed in animals receiving injections of histamine or of ascaris extract. An increased number of eosinophiles was first noted in the blood stream and next in the perivascular connective tissues of the lung. They gradually migrated to the wall and lumen of the bronchi where they entered the lymphatic system and were eventually found in the splenic pulp. The histamine reactions differed slightly from the ascaris one in that the eosinophile response appeared somewhat more rapidly and was accompanied by the migration to the lungs of neutrophiles as well as eosinophiles. The tissues of guinea pigs with natural eosinophilia (secondary to worm infestation) were similar to those of the animals with experimental eosinophilia. It is suggested that the function of the eosinophilic leukocyte is to transport histamine or an H-like noxious material to the tissues for inactivation and that the results obtained in guinea pigs foreshadow what takes place in human beings. R. W.

Paper Electrophoresis of Serum Proteins. With Micro-Kjeldahl Nitrogen Analysis of the Protein Fractions. A Comparison With Free Electrophoresis and Salt Fractionation Methods. Levin, B., and Oberholzer, V. G.: Am. J. Clin. Path. **23**: 205, 1953.

The technique for paper electrophoresis of serum is described. Comparative data are presented for 7 sera compared with the usual Tiselius electrophoresis determination and for 17 sera compared with the salt-fractionation method. The advantages for paper electrophoresis are that only a small amount of serum is necessary; several sera may be analyzed simultaneously in one apparatus and at room temperature; no preliminary dialysis is necessary; and very milky sera can be analyzed readily. "It is concluded that paper electrophoresis is to be preferred to salt-fractionation methods, and that on the grounds of simplicity, nitrogen analysis following paper electrophoresis is preferable to dye elution." K.

The Use of Neo-Penil, A Diethylaminoethyl Ester of Penicillin, In Pulmonary Disease. Dulfano, M. J., and Segal, M. S.: Dis. Chest **23**: 136, 1953.

Forty-eight patients with acute or chronic pulmonary disease received Neo-Penil in doses from 500,000 to 1,000,000 units daily for from five to twelve days. Among this series, there were 10 with chronic bronchial asthma and pulmonary infection, 9 with lobar pneumonia, 6 with acute and chronic bronchitis, 5 with pneumonitis, 4 with chronic pulmonary emphysema, 4 with bronchiectasis, 4 with bronchopneumonia, and 1 each with tuberculosis, sialolithiasis, bilateral maxillary sinusitis, acute pleurisy, pneumoconiosis, and atelectasis. The ages ranged from 6 months to 77 years. Patients were observed for objective changes, such as temperature, amount of expectoration, intensity and character of cough, variations in bacterial flora, and roentgenographic changes. Temperatures became normal in all but 6 cases. The daily amount of expectoration was significantly decreased in all but 3, and cough was uniformly decreased in all patients. The conversion of bacterial flora lagged behind clinical results. The appearance of new bacterial flora at the end of treatment did not alter the beneficial clinical results. No significant toxic or untoward effects were noted during or after Neo-Penil therapy. In general, the clinical results were excellent in 9 cases, good in 22, fair in 9, and poor in 8. In comparative studies of blood and sputum levels of penicillin following single intramuscular injections of Neo-Penil in doses of 300,000, 500,000, and 1,000,000 units, peak levels in the sputum were consistently higher than those found in the blood serum. It was concluded that Neo-Penil appeared to be an effective preparation for pulmonary diseases whenever a high local concentration of the drug in the lung was desired. E. W.

Drug Fever Due to Quinidine. Rose, O. A., Vogl, A., and Turtz, A. L.: New England J. Med. **248**: 96, 1953.

Three cases were observed in which fever, ranging up to 104° F., occurred following quinidine administration. In each patient, the fever was associated with a macular eruption, which was often pruritic. In two instances, vomiting and tinnitus were also present. The febrile reactions occurred shortly after the administration of the second course of quinidine in 2 patients and in the third after the drug had been administered for two weeks. In one case, a positive skin reaction was obtained following an intracutaneous test with 0.1 Gm. of quinidine hydrochloride. A similar test performed on a normal subject gave a negative reaction. B. S.

Lipid Deposition in Aortas in Younger Age Groups Following Cortisone and Adrenocorticotrophic Hormone. Etheridge, E. M., and Hoch-Ligeti, C.: Am. J. Path. **28**: 315, 1952.

The aortas of 33 patients under 21 years of age, who had been treated with cortisone or ACTH and who subsequently came to autopsy, were studied and compared with a suitable control group. Most of these patients had died of leukemia.

An increased deposit of lipid was found in the intima and media of patients under 11 years of age who received cortisone or ACTH. After the age of 11, lipid was frequently found in the control group so that comparison of the two groups was not reliable. The degree of lipid deposition was not related to the amount of hormone received, but there seemed to be some relation to the duration of treatment. No difference could be detected between the effects of cortisone and ACTH. J. S.

Effect of Histoplasmin Skin Testing on Serologic Results. Saslow, S., and Campbell, C. C.: Proc. Soc. Exper. Biol. & Med. **82**: 689, 1953.

Normal medical students received 6 weekly intracutaneous injections of 0.1 ml. of histoplasmin. Antibodies developed in most of the skin-test positive subjects after the second skin test, while more appeared in skin-test negative individuals. The antibody response was measured by the collodion agglutination test and a complement-fixation test with either histoplasmin yeast phase antigen or histoplasmin. The latter proved to be the more sensitive test. With this technique, the sera of 85 per cent of the cases showed the presence of antibodies to histoplasmin, which persisted in some cases as long as thirty-nine weeks. A transient response was obtained in complement-fixation studies with cross-reacting yeast phase blastomyces antigen, but not with coccidiodin antigen.

Since no serologic alterations occurred in skin-test negative individuals, it was assumed that in the positive skin reactors a previous immune response was recalled by skin testing. It is suggested that repeated histoplasmin skin testing of skin-test positive individuals may invalidate the results of diagnostic serologic tests for histoplasmosis. M. Cohen.

Specificity of Auto-Antibodies in Hemolytic Anemia. Davidsohn, I., and Oyamada, A.: Am. J. Clin. Path. **23**: 101, 1953.

The antiglobulin (Coombs) test and warm and cold agglutinin determinations were carried out on patients with various kinds of hemolytic anemia. Titrations were done using "the patients' own cells, cells of the same group and Rh type as the patients', and cells of group O of the same Rh type as the patients', . . ." Other cells (opposite Rh type) were sometimes used. The techniques employed are described in detail and included the use of papain-treated cells. Three reaction patterns were found. In 11 cases, no difference was detected in the titer of autoagglutinins when the different red cells were used. In 4 cases, the titer for the patients' own cells was respectively 4, 4, 8, and 1,000 fold that for cells other than those of group O. The group O cells showed a titer as high as the patients' own cells. In a third group of 11 cases, cells of other persons failed to react at all whereas the patients' own cells showed varying titers, usually relatively high. These patterns remained quite consistent over a ten- to eleven-month observation period. Papain increased red cell sensitivity, but, in only 2 of 8 cases, did it change the above reaction pattern. There was no correlation between the above reaction patterns and the severity of the anemia. In 8 of 13 cases of idiopathic acquired hemolytic anemia, the direct quantitative antiglobulin test showed titers of 1:64 or higher while 6 of 7 patients with symptomatic anemia showed titers of 1:4 or lower. In idiopathic acquired hemolytic anemia, the failure of patients' serum to clump cells other than their own was particularly frequent. "The antiglobulin test was positive in 32 of 33 patients . . . with acquired idiopathic anemia, in 14 of 28 patients . . . with symptomatic hemolytic anemia and in 3 of 14 patients . . . with hereditary spherocytosis. The incidence of warm autoagglutinins in these patients was 61, 25 and 1 per cent, respectively. . . ." K.